

Application No.: 09/735,574

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) A computer implemented method for calculating a normalization factor comprising:

providing a first intensity value ($I^{(1)}$) of a probe in a first probe array and a second intensity value ($I^{(2)}$) of said probe in a second probe array, wherein the intensity values indicate nucleic acid hybridization;

obtaining the geometric mean (x) of said $I^{(1)}$ and said $I^{(2)}$;

calculating said normalization factor according to:

$f(x) = e^{h(x)}$, wherein said $h(x)$ is derived from referential intensities from said first and second probe arrays; and

Using said normalization factor for gene expression analysis and outputting the result of said analysis.
2. (original) The method of Claim 1 wherein said $h(x)$ is derived by relating geometric means (x_i) of first referential intensities ($RI_i^{(1)}$) in the first probe array and second referential intensities ($RI_i^{(2)}$) in the second probe array to:

$$y_i = \log \left(\frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$
3. (original) The method of Claim 2 wherein said relating comprising:

Application No.: 09/735,574

sorting (x_i, y_i) pairs according to x_i into a plurality (m number) of bins with no overlapping;

computing medians (\bar{x}_k) of x_i 's and medians (\bar{y}_k) of y_i 's for each bin; and

interpolating said medians (\bar{x}_k, \bar{y}_k).

4. (original) The method of Claim 3 wherein said bins are of approximately equal size.

5. (original) The method of Claim 4 wherein said $h(x)$ is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_1 + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_i + 1), w = \frac{\bar{x}_i + 1 - x}{\bar{x}_i + 1 - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

6. (original) The method of Claim 5 wherein said m is 3.

7. (withdrawn) A computer implemented method for comparing the expression of a gene in a first sample with a second sample comprising:

providing a first plurality of intensity values ($I_i^{(1)}$), each of which reflects the expression of said gene in said first sample, wherein said intensity values are obtained from a first nucleic acid probe array;

Application No.: 09/735,574

providing a second plurality of intensity values ($I_i^{(2)}$), each of which reflects the expression of said gene in said second sample, wherein said intensity values are obtained from a second nucleic acid probe array;

calculating a p -value using one-sided Wilcoxon's signed rank test, wherein the p -value is for a null hypothesis that $median(f(x) I_i^{(2)} - I_i^{(1)}) = 0$ and an alternative hypothesis that $median(f(x) I_i^{(1)} - I_i^{(2)}) > 0$, wherein said $f(x)$ is a normalization factor; and

indicating whether said transcript is present based upon said p -value.

8. (withdrawn) The method of Claim 7 further comprising a step of calculating normalization factor, said step comprising:

obtaining the geometric mean (x) of said $I_i^{(1)}$ and said $I_i^{(2)}$;

calculating said normalization factor according to:

$f(x) = e^{h(x)}$, wherein said $h(x)$ is derived from referential intensities from said first and second probe arrays.

9. (withdrawn) The method of Claim 8 wherein said $h(x)$ is derived by relating geometric means (x_i) of first referential intensities ($RI_i^{(1)}$) in said first probe array and said second referential intensities ($RI_i^{(2)}$) in said second probe array to:

$$y_i' = \log \left(\frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

10. (withdrawn) The method of Claim 9 wherein said relating comprising:

Application No.: 09/735,574

sorting (x_i, y_i) pairs according to x_i into a plurality (m number) of bins with no overlapping;

computing medians (\bar{x}_k) of x_i 's and medians (\bar{y}_k) of y_i 's for each bin; and

interpolating said medians (\bar{x}_k, \bar{y}_k) .

11. (withdrawn) The method of Claim 10 wherein said bins are of approximately equal size.

12. (withdrawn) The method of Claim 11 wherein said $h(x)$ is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_i + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_{i+1}], w = \frac{\bar{x}_{i+1} - x}{\bar{x}_{i+1} - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

13. (withdrawn) The method of Claim 12 wherein said m is 3.

14. (currently amended) A system for calculating a normalization factor comprising:

a processor; and

a memory coupled with the processor, the memory storing a plurality of machine instructions that cause the processor to perform a plurality of logical steps when implemented by the processor, the logical steps comprising:

providing a first intensity value ($I^{(1)}$) of a probe in a first probe array and a second intensity value ($I^{(2)}$) of said probe in a second probe array, wherein the intensity values indicate nucleic acid hybridization;

Application No.: 09/735,574

obtaining the geometric mean (x) of said $I^{(1)}$ and said $I^{(2)}$;

calculating said normalization factor according to:

$f(x) = e^{h(x)}$, wherein said $h(x)$ is derived from referential intensities from

said first and second probe arrays; and

using said normalization factor for gene expression analysis and outputting the result of said analysis.

15. (original) The system of Claim 14 wherein said $h(x)$ is derived by relating geometric means (x_i) of first referential intensities ($RI_i^{(1)}$) in the first probe array and second referential intensities ($RI_i^{(2)}$) in the second probe array to:

$$y_i = \log \left(\frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

16. (original) The system of Claim 15 wherein said relating comprising:
 sorting (x_i, y_i) pairs according to x_i into a plurality (m number) of bins with no overlapping;
 computing medians (\bar{x}_k) of x_i 's and medians (\bar{y}_k) of y_i 's for each bin; and
 interpolating said medians (\bar{x}_k, \bar{y}_k).

17. (original) The system of Claim 16 wherein said bins are of approximately equal size.

18. (original) The system of Claim 17 wherein said $h(x)$ is:

Application No.: 09/735,574

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_i + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_{i+1} + 1), w = \frac{\bar{x}_{i+1} + 1 - x}{\bar{x}_{i+1} + 1 - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

19. (original) The system of Claim 18 wherein said m is 3.
20. (withdrawn) A system for comparing the expression of a gene in a first sample with a second sample comprising:
 - a processor; and
 - a memory coupled with the processor, the memory storing a plurality of machine instructions that cause the processor to perform a plurality of logical steps when implemented by the processor, the logical steps comprising:
 - providing a first plurality of intensity values ($I_i^{(1)}$), each of which reflects the expression of said gene in said first sample, wherein said intensity values are obtained from a first nucleic acid probe array;
 - providing a second plurality of intensity values ($I_i^{(2)}$), each of which reflects the expression of said gene in said second sample, wherein said intensity values are obtained from a second nucleic acid probe array;
 - calculating a p -value using one-sided Wilcoxon's signed rank test, wherein the p -value is for a null hypothesis that $\text{median}(f(x) I_i^{(2)} - I_i^{(1)}) = 0$ and an alternative hypothesis that $\text{median}(f(x) I_i^{(1)} - I_i^{(2)}) > 0$, wherein said $f(x)$ is a normalization factor; and
 - indicating whether said transcript is present based upon said p -value.

Application No.: 09/735,574

21. (withdrawn) The system of Claim 20 further comprising a step of calculating normalization factor, said step comprising:

obtaining the geometric mean (x) of said $I_i^{(1)}$ and said $I_i^{(2)}$;

calculating said normalization factor according to:

$f(x) = e^{h(x)}$, wherein said $h(x)$ is derived from referential intensities from said first and second probe arrays.

22. (withdrawn) The system of Claim 21 wherein said $h(x)$ is derived by relating geometric means (x_i) of first referential intensities ($RI_i^{(1)}$) in said first probe array and said second referential intensities ($RI_i^{(2)}$) in said second probe array to:

$$y_i = \log\left(\frac{RI_i^{(1)}}{RI_i^{(2)}}\right).$$

23. (withdrawn) The system of Claim 22 wherein said relating comprising: sorting (x_i, y_i) pairs according to x_i into a plurality (m number) of bins with no overlapping;

computing medians (\bar{x}_k) of x_i 's and medians (\bar{y}_k) of y_i 's for each bin; and

interpolating said medians (\bar{x}_k, \bar{y}_k).

24. (withdrawn) The system of Claim 23 wherein said bins are of approximately equal size.

Application No.: 09/735,574

25. (withdrawn) The system of Claim 24 wherein said $h(x)$ is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_i + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_{i+1} + 1], w = \frac{\bar{x}_{i+1} - x}{\bar{x}_{i+1} - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

26. (withdrawn) The system of Claim 25 wherein said m is 3.

27. (currently amended) A computer software product for calculating a normalization factor comprising:

computer program code for providing a first intensity value ($I^{(1)}$) of a probe in a first probe array and a second intensity value ($I^{(2)}$) of said probe in a second probe array, wherein the intensity values indicate nucleic acid hybridization;

computer program code for obtaining the geometric mean (x) of said $I^{(1)}$ and said $I^{(2)}$;

computer program code for calculating said normalization factor according to:

$f(x) = e^{h(x)}$, wherein said $h(x)$ is derived from referential intensities from said first and second probe arrays; and

computer program code for using said normalization factor for gene expression analysis and outputting the result of said analysis; and

a computer readable medium for storing said codes.

Application No.: 09/735,574

28. (original) The computer software product of Claim 27 wherein said $h(x)$ is derived by relating geometric means (x_i) of first referential intensities ($RI_i^{(1)}$) in the first probe array and second referential intensities ($RI_i^{(2)}$) in the second probe array to:

$$y_i = \log \left(\frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

29. (original) The computer software product of Claim 28 wherein said code for relating comprising:
- computer program code for sorting (x_i, y_i) pairs according to x_i into a plurality (m number) of bins with no overlapping;
- computer program code for computing medians (\bar{x}_k) of x_i 's and medians (\bar{y}_k) of y_i 's for each bin; and
- computer program code for interpolating said medians (\bar{x}_k, \bar{y}_k).

30. (original) The computer software product of Claim 29 wherein said bins are of approximately equal size.

31. (original) The computer software product of Claim 30 wherein said $h(x)$ is:

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_1 + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_{i+1}), w = \frac{\bar{x}_{i+1} - x}{\bar{x}_{i+1} - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

Application No.: 09/735,574

32. (original) The computer software product of Claim 31 wherein said m is 3.
33. (withdrawn) A computer software product for comparing the expression of a gene in a first sample with a second sample comprising:
- computer program code for providing a first plurality of intensity values ($I_i^{(1)}$), each of which reflects the expression of said gene in said first sample, wherein said intensity values are obtained from a first nucleic acid probe array;
 - computer program code for providing a second plurality of intensity values ($I_i^{(2)}$), each of which reflects the expression of said gene in said second sample, wherein said intensity values are obtained from a second nucleic acid probe array;
 - computer program code for calculating a p -value using one-sided Wilcoxon's signed rank test, wherein the p -value is for a null hypothesis that $median(f(x) I_i^{(2)} - I_i^{(1)}) = 0$ and an alternative hypothesis that $median(f(x) I_i^{(1)} - I_i^{(2)}) > 0$, wherein said $f(x)$ is a normalization factor;
 - computer program code for indicating whether said transcript is present based upon said p -value; and
 - a computer readable medium for storing said codes.
34. (withdrawn) The computer program code of Claim 33 further comprising computer program code for calculating normalization factor, said code comprising:
- code for obtaining the geometric mean (x) of said $I_i^{(1)}$ and said $I_i^{(2)}$;

Application No.: 09/735,574

code for calculating said normalization factor according to:

$$f(x) = e^{h(x)}, \text{ wherein said } h(x) \text{ is derived from referential intensities from}$$

said first and second probe arrays.

35. (withdrawn) The computer software product of Claim 34 wherein said $h(x)$ is derived by relating geometric means (x_i) of first referential intensities ($RI_i^{(1)}$) in said first probe array and said second referential intensities ($RI_i^{(2)}$) in said second probe array to:

$$y_i = \log \left(\frac{RI_i^{(1)}}{RI_i^{(2)}} \right).$$

36. (withdrawn) The computer software product of Claim 35 wherein said code for relating comprising:
- computer code for sorting (x_i, y_i) pairs according to x_i into a plurality (m number) of bins with no overlapping;
- computer code for computing medians (\bar{x}_k) of x_i 's and medians (\bar{y}_k) of y_i 's for each bin; and
- computer code for interpolating said medians (\bar{x}_k, \bar{y}_k).

37. (withdrawn) The computer software product of Claim 36 wherein said bins are of approximately equal size.

38. (withdrawn) The computer software product of Claim 37 wherein said $h(x)$ is:

Application No.: 09/735,574

$$h(x) = \begin{cases} \bar{y}_1, & \text{if } x \leq \bar{x}_1 \\ w\bar{y}_i + (1-w)\bar{y}_{i+1}, & \text{if } x \in (\bar{x}_i, \bar{x}_i + 1], w = \frac{\bar{x}_{i+1} - x}{\bar{x}_{i+1} - \bar{x}_i}, i = 1, \dots, m-1, \\ \bar{y}_m, & \text{if } x > \bar{x}_m. \end{cases}$$

39. (withdrawn) The computer software product of Claim 38 wherein said m is 3.